REMARKS

I. Status of the Claims

Claims 245-248, 251, 253, 261-265, 306 and 307 were pending and examined in the August 17, 2010 Office Action. Claims 245, 247, 263, 306, and 307 are amended herewith. The claim amendments are made without prejudice or disclaimer and provide no new matter. Claims 245-248, 251, 253, 261-265, 306 and 307 are presented for reconsideration.

I. Double Patenting Rejections

Claims 245-248, 251, 253, 261-265, 306 and 307 are provisionally rejected on the ground of obviousness-type double patenting (ODP) as being unpatentable over claims 275, 289, 290 and 296-301 of copending Application No. 08/978,634. Additionally, claims 245-248, 251, 253, 261-265, 306 and 307 are provisionally rejected on the ground of ODP as being unpatentable over claims 1 and 3-5 of copending Application No. 11/929,897. Since these rejections are dependent on the scope of the final claims in both the instant application and application 08/978,634, Applicants will provide a terminal disclaimer where necessary when a proper ODP rejection is the only rejection remaining in this application.

II. Rejection under 35 U.S.C. § 112, First Paragraph – Written Description

Claims 245-251, 253, 261-265, 306 and 307 are rejected under 35 U.S.C. 112, first paragraph, written description requirement. Applicants request reconsideration and withdrawal of this rejection in light of the following discussion.

The current claims are directed to compositions that comprise (a) various nucleic acid configurations that include a sequence that is a template for synthesis of a nucleic acid product, and (b) a non-nucleic acid component. Methods of introducing these compositions into cells are also claimed. Specific examples of these compositions, and methods of making portions of same, are illustrated in FIGS. 4-6.

While the Office Action asserts that the claimed genus of nucleic acid constructs "...reads on a broad array of structures (e.g. thousands and thousands of structures), and the disclosure fails to provide a representative number of species for such a broad genus providing cell delivery to any cell in an organism in vivo or in vitro" (Office Action at page 6), Applicants assert that the instant claims are fully described in the specification such that the skilled artisan would understand that the inventors possessed the claimed invention for its full scope.

The specification provides an extensive disclosure of each aspect of the claimed methods, as follows, referring to the specification as published in Publication No. 2001/0006841. A discussion of non-nucleic acid components, including binders, as recited in the instant claims is provided at least at paragraphs 108-113 (p. 7), 121-139 (p. 8-9), 157-158 (p. 9-10), 203-216 (p. 14), 220-243 (p. 14-16), and 402-410 (p. 29-30). Additionally, the metes and bounds of the nucleic acid components is provided at least at paragraphs 114-120. Domains are described at least at paragraphs 159-171 (p. 11). Methods for attaching the non-nucleic acid components are provided at least at paragraphs 180-189 (p. 12-13). The particular configurations of the claimed compositions is described at least at paragraphs 117 (p. 8) and 383-395 (Examples 5 and 6 on pp. 26-27). Thus, each element of the claimed compositions and methods, as well as specific examples of those compositions and methods are literally described in the specification.

The claims precisely define the metes and bounds of the claimed compositions and methods. While the Office Action asserts that "[c]oncise structural features that would distinguish structures within the broadly claimed genus of sequences are missing from the disclosure," pointing to detailed questions of "[h]ow many nucleotide residues are required... etc." (Office Action, pp. 6-7), Applicants assert that the state of the art of molecular biology at the time of filing was very predictable. The skilled artisan would thus understand that the answers to the questions poised in the Office Action for any particular target nucleic acid and non-nucleic acid component within the scope of the claims would be understood, or could be achieved with only routine experimentation. In

this regard, Applicants remind the Office that "[w]hat is conventional or well known to one of ordinary skill in the art need not be disclosed in detail." MPEP 2163 II.A.3.(a). Thus, while the current claims do indeed encompass "thousands and thousands of structures," those claims are directed to compositions that are combinations of multiple molecular biology elements in a novel and nonobvious combination, where the behavior of each element is thoroughly predictable in light of the state of the art.

As examples of relevant state of the art, Applicants point to the following references describing nucleic acid/non-nucleic acid complexes, where the non-nucleic acid component directs the nucleic acid component for targeted gene expression.

- Wu et al., 1994, J. Biol. Chem. 269:11542-6, describing a DNA complexed with an asialoglycoprotein-polylysine-adenovirus that had increased transfection of cells *in vitro*.

- Ferkol et al., 1995, J. Clin. Invest., describing a complex of an Fab portion of antibodies with DNA that targeted expression of the DNA to the airway epithelium of animals *in vivo*.

- Cristiano et al., 1993, describing an asialoorosomucoid-DNA complex resulting in a high level of gene expression in hepatocytes.

- Hirsch et al., 1993, Transplantation Proceedings 25:138-9, describing the use of antibody-DNA conjugates for targeting gene expression.

All of the above references have been provided in Information Disclosure Statements in the instant application.

The Office Action further asserts that "no reductions to practice have been provided for the instant schematics, whereby the proposed structures are successfully targeted to, and transfected into target cells, remain intact as schematically depicted, and produce the recombinant nucleic acids or protein expression products in a predictable manner." (Office Action at p. 6). In response, Applicants note that the specification provides 32 examples providing detailed methods for producing and testing various aspects of the instant claims. While the examples are prophetic, the routine state of the art of molecular biology at the time of filing would give the skilled

artisan confidence that the methods recited therein are functional. Applicants also note that evidence of actual reduction to practice need not be provided to satisfy the written description requirement: "An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention." MPEP 2163 II.A.3.(a). In the present case, the extensive description in the specification including descriptions of each element of the claims and examples of the specifically claimed embodiments, and the routine nature of the state of the art would lead the skilled artisan to conclude that the Applicants had possession of the claimed compositions and methods at the time of filing.

In view of the above discussion, withdrawal of the written description rejection under 35 U.S.C. 112, first paragraph, is respectfully requested.

III. Rejection under 35 U.S.C. § 112, First Paragraph – Enablement

Claims 245-251, 253, 261-265, 306 and 307 are rejected under 35 U.S.C. 112, first paragraph, enablement requirement. Applicants respectfully request reconsideration and withdrawal of this rejection in light of the following discussion.

The Office Action provides six references purporting to establish the unpredictability of the instant claims. Applicants first note, however, that five of those references only discuss the predictability of antisense therapeutics, whereas the instant claims are not so limited. For example, claim 245 only recites that "said double-stranded portion forms a template for synthesis of a nucleic acid product when present in a cell." Additionally, claim 247 and 306 recites that "said specific nucleic acid component is a nucleic acid construct that directs synthesis of a nucleic acid product". The claims have no requirement that the nucleic acid product synthesized in the cell be an antisense, only that it is synthesized in a cell. The skilled artisan would understand that the product could be an mRNA that is further translated into a protein. The product could also simply be a marker that indicates cells transfected with the composition.

In further regard to the five references that the Office Action purports to establish the unpredictability of the instant claims, Applicants note that the Office Action indicates that the unpredictability of the antisense methods described in those references is primarily due to targeting and delivery issues. In this regard, Applicants point out that the non-nucleic acid component of the claimed compositions specifically addresses targeting and delivery of the nucleic acids. See, e.g., paragraphs 123-138 on pp. 8-9 of the specification as published in US 2001/0006418. Thus, the instant compositions and methods directly address the issues that the Office Action asserts are the reasons that antisense technology was unpredictable at the time of filing. That the non-nucleic acid component does effectively address those purported causes of unpredictability is established by literature present at the time of filing, for example the four references referred to under **II.** above.

The Office Action also provides Jang at al. as providing further evidence of the unpredictability of the instant claims. However, that reference, referring to gene delivery from polymer scaffolds for tissue engineering, is completely irrelevant to the instant claims, since the instant claims are not directed to gene delivery from polymer scaffolds.

Applicants further note that all of the instant claims except for 263-265 and 307 are directed to compositions and not methods. The Office Action does not provide any indication that the compositions are not enabled, and Applicants assert that those compositions as claimed can be prepared without undue experimentation.

The Office Action further asserts that the claims are not enabled for *in vivo* embodiments. In response, Applicants again note that the claims only require that the compositions be delivered to cells such that the nucleic acid product is synthesized. There is no further requirement in the claims. As such, the skilled artisan would understand how to make and use the instant compositions such that the nucleic acid product would likely be synthesized in cells *in vivo*. Such an enablement is further supported by the Ferkol et al. reference cited in **II.** above, where the antibody component of the composition described therein allowed the expression of an antibody-vector complex *in vivo*.

In view of the above discussion, Applicants assert that the claims are enabled for their full scope. Withdrawal of the enablement rejection under 35 U.S.C. 112, first paragraph, is therefore respectfully requested.

IV. Conclusion

In view of the foregoing remarks, Applicants respectfully request withdrawal of rejections of record and passage of the claims to allowance.

Applicants authorize the United States Patent and Trademark Office to charge all fees required to maintain pendency of this application, including the extension of time, to Deposit Account No. 05-1135.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney requests that he be contacted at the number provided below.

Respectfully submitted,

Elie Gendloff
Registration No. 44,704
Attorney for Applicants

ENZO BIOCHEM, INC.
527 Madison Avenue, 9th Floor
New York, New York 10022-4304
Telephone: (212) 583-0100
Facsimile: (212) 583-0150